80. The isolated nucleic acid molecule of claim 68, which is fused to a polynucleotide encoding a heterologous protein.

81. A method of making a recombinant vector comprising inserting the nucleic acid molecule of claim 68 into a vector.

82. A recombinant vector produced by the method of claim 81.

83. A genetically engineered host cell that contains the nucleic acid molecule of claim 82.

84. A genetically engineered host cell that contains the polynucleotide of claim 68 operatively associated with a regulatory sequence that controls gene expression.

85. A recombinant method for producing a polypeptide, comprising culturing the host cell of claim 84 under conditions such that said polypeptide is expressed and recovering said polypeptide.--

Remarks

Claims 21-29 and 32-34 have been canceled in favor of new claims 36-85 in order to more precisely define the invention. Claims 31 and 36-85 are pending. Applicants appreciate the Examiner's allowance of claim 31. New claims 36-85 find support throughout the specification and originally filed claims. Specifically, support for claims 36-85 can be found in specification at

page 6, lines 9-14 and 29-33; page 8, line 22 to page 9, line 17; page 9, last paragraph; page 10, line 20 to page 11, line 4; page 11, last paragraph to page 12, first paragraph; page 12, line 26 to page 13, line 6; page 33, lines 18-27.

Support for new claims 43-45 can be found in original claim 1 and SEQ ID NO:1. In particular, the ATG codon that encodes the first amino acid residue (Met) of the TNFR polypeptide sequence is at positions 46-48 in SEQ ID NO:1. Similarly, TTA, the codon that encodes the last amino acid residue (Leu) of the polypeptide sequence is at positions 1246-1248 in SEQ ID NO:1. Thus, the nucleotides that encode the first and last amino acid residues of the TNFR polypeptide are specifically indicated by the specification. Further, previous claim 21(a) recites "a polynucleotide sequence encoding a polypeptide comprising amino acids -21 to 380 in SEQ ID NO:2." The first nucleotide of the codon that encodes amino acid number -21 in SEQ ID NO:2 is at position 46 of SEQ ID NO:1 and the last nucleotide of the codon that encodes amino acid number 380 in SEQ ID NO:2 is at position 1248 in SEQ ID NO:1. Claim 21(b) recites "a nucleotide sequence encoding a polypeptide comprising amino acids -20 to 380 in SEQ ID NO:2." The first nucleotide of the codon that encodes amino acid number -20 in SEQ ID NO:2 is at position 49 of SEQ ID NO:1 and the last nucleotide of the codon that encodes amino acid number 380 in SEQ ID NO:2 is at position 1248 in SEQ ID NO:1. In addition, claim 21(c) recites "a nucleotide sequence encoding a polypeptide comprising amino acids 1 to 380 in SEQ ID NO:2." The first nucleotide of the codon that encodes amino acid number 1 in SEQ ID NO:2 is at position 109 of SEQ ID NO:1 and the last nucleotide of the codon that encodes amino acid number 380 in SEQ ID NO:2 is at position 1248 in SEQ ID NO:1. Accordingly, it is clear that the skilled artisan would have understood the present inventors to have been in possession of the subject matter of claims 43-45.

In other words, since, for example, the Examiner has already acknowledged that there is support for the subject matter of previous claim 21(a) (i.e., a polynucleotide encoding a polypeptide comprising amino acids -21 to 380 of SEQ ID NO:2), there must also be support for nucleotides 46 to 1248 of SEQ ID NO:1, since these are the nucleotides that encode amino acids -21 to 380.

In addition, the specification has been amended to correctly reflect the priority application data as well as the current address of the ATCC. Thus, no new matter has been added by way of amendment to the specification or claims.

Consideration of References Cited in the Information Disclosure Statement

Applicants note that the Examiner has struck certain references (AR7, AS7, AS8, AT8, AR9, AS2, AR10, AS10, AT10 and AR11) from the First Supplemental Information Disclosure Statement Form 1449 filed April 18, 1997, "because they are not journals, patents or publications."

The documents "struck through" by the Examiner include GenBank releases and International Search Reports. As indicated previously, contrary to the Examiner's position, neither the 37 CFR Rules nor the MPEP require that the "information" be in a particular form. Thus, it is respectfully submitted that the Examiner was under an obligation to consider all references that accompanied the First Supplemental IDS filed April 18, 1997. However, in accordance with the Examiner's request, the GenBank releases are cited in the PTO-1449 accompanying the Second Supplemental Information Disclosure Statement submitted herewith as documents AS11, AT11, AR12, AS12, AT12, AR13 and AS13, respectively. Applicants again respectfully request that the Examiner consider these references.

It has been Applicants previous experience that GenBank releases are routinely considered by other USPTO Examiners when timely submitted in an IDS. Thus, Applicants are somewhat confused as to the Examiner's reluctance to consider these references. The Examiner suggests that Applicants submit "a clear and concise explanation of the references . . ." However, the Examiner cites no 37 CFR Rule or passage from the MPEP where this is required. In fact, the MPEP appears to require such a "concise explanation" only when the submitted information is not in the English language. *See* MPEP §609 A(3).

The International Search Reports (ISRs)are cited in the PTO-1449 accompanying the Second Supplemental Information Disclosure Statement submitted herewith as documents AS18, AT18 and AR19. Again, Applicants are somewhat confused as to the Examiner's reluctance to consider these reports. The ISRs are prepared by the PCT Office and include the impressions of the PCT Examiner concerning the relevance of the documents cited therein. Thus, Applicants believe that the present Examiner would find the reports helpful and submit them as a courtesy.

Objections

The Examiner objected the amendment filed on May 28, 1997 (Paper No. 17) under 35 U.S.C. § 132 because it allegedly introduces new matter. In particular, it is the Examiner's position that the "[a]mendment to page 6, lines 26-27, which changes "39%" to "about 27%", "46%" to "about 43%", and "an 88 amino acid stretch" to "the entire length of the proteins" is not supported by the specification." Applicants disagree. The percentage of sequence homology of the present protein to the human type 2 TNF receptor is an inherent property of the two sequences. Thus, the original percent identity and percent similarity figures necessarily changed

due to the sequence correction filed with the Response on May 28, 1997. However, since the sentence at page 6, lines 24-27, of the specification is not necessary for practicing the invention, Applicants have deleted this sentence to obviate the objection. Therefore, it is respectfully requested that it be withdrawn.

The Examiner also objected to the amendment on page 1 of the specification, which indicated that the present application claimed priority to PCT/US95/03216. To obviate this objection, Applicants have canceled the statement "which is relied upon and incorporated by reference in its entirety." Accordingly, it is respectfully requested that the objection be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 21-29 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

In particular, it is the Examiner's position that there is no written descriptive support in the specification for the recitation "amino acids -20 to 380 of SEQ ID NO:2." Applicants respectfully disagree and traverse this rejection as applied to currently pending claims 36 (b) and 44.

The examiner is reminded that the adequate written description requirement serves to ensure that the inventors had possession, as of the filing date, of the claimed subject matter. However, "how the specification accomplishes this is not material." *In re Wertheim*, 191 USPQ

90, 96 (CCPA 1976). Further, in a case involving whether there was adequate written description in a specification for claiming an analog of IFN-γ, the Federal Circuit stated that "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met." *In re Alton*, 37 USPQ 2d 1578, 1584 (CAFC 1996). Thus, in the present situation, the standard for adequate written descriptive support is not whether the numbers "-20 to 380" appear in the specification, but instead is whether a person of ordinary skill would have understood the present inventors to have been in possession of the claimed subject matter, i.e., a polynucleotide encoding a polypeptide comprising amino acids -20 to 380 of SEQ ID NO:2.

The recitation "amino acids -20 to 380 of SEQ ID NO:2" refers to a polypeptide wherein the initial methionine residue has been removed. Support for this can be found in the specification on page 19, lines 20-21, wherein it states: "[p]olypeptides of the invention *may* also include an initial methionine amino acid residue." (Emphasis added). By stating that polypeptides of the present invention *may* have an initial methionine, the inventors were clearly contemplating polypeptides that lack an initial methionine as well as polypeptides that include an initial methionine. Accordingly, it is clear that the skilled artisan would have understood the present inventors to have been in possession of a polynucleotide encoding the polypeptide of SEQ ID NO:2 that lacks the initial methionine. Thus, it is respectfully requested that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 21-29 and 31-34 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Particularly, the Examiner argued that the recitation of "% identity" renders the claims indefinite because the algorithm used to calculate sequence identity has not been defined in the specification. Applicants respectfully disagree with the Examiner's reasoning and traverse this rejection as applied to claims 21-29 and 31-34 as well as the currently pending claims.

The test for indefiniteness is whether the scope of the claim is clear to a hypothetical person possessing an ordinary level of skill in the pertinent art. (M.P.E.P. § 2171.) The language of the claim must reasonably apprise those skilled in the art both of the utilization and the scope of the invention. (*PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558 (Fed. Cir. 1996.) In interpreting language used in a claim, words are to be given their ordinary meaning in the absence of indication in the patent to the contrary. (*Markman v. Westview Instr., Inc.*, 52 F.3d 967 (Fed. Cir. 1995)(in banc) *aff'd*, 116 S.Ct. 1384 (1996).)

Applicants firmly assert that the term "identity" is clear on its face. The plain and ordinary meaning of the word "identity," as defined by Merriam-Webster's Collegiate Dictionary, Tenth Edition (1997), is (a) "sameness of essential or generic character in different instances" or (b) "sameness in all that constitutes the objective reality of a thing." (Copy enclosed.) Thus, if a claim were to recite "identity" alone or "100% identity," a reference sequence and a second sequence would be identical when aligned. Similarly, where a reference polynucleotide is 100 nucleotides in length and the claim recites "at least 95% identical", the plain and ordinary meaning is that at least 95 out of 100 comparison events (i.e., nucleotide comparison events) must be

identical for a second polynucleotide to fall within the claim. In other words, the claims allow for less than or equal to 5% differences between the reference sequence and a second sequence. Any difference, including any addition, deletion, or substitution, between the reference sequence and the second sequence are counted as non-identity events when determining the % identity between two sequences. (These differences are fully described in the specification - e.g., see page 8, lines, 9-11, wherein it states "[S]uch nucleotide variants include deletion variants, substitution variants and addition or insertion variants." Further support for such alterations in the nucleotide sequence are found in the specification at page 8, lines 15-20.)

Thus, if the reference sequence and a second sequence have less than or equal to 5% differences - or 5 out of 100 nucleotide differences - then the second sequence falls within the scope of the claim. If there are more than 5 out of 100 nucleotide differences, the second sequence is not encompassed by the claim. Accordingly, Applicants believe that the language "at least 95% identity" would reasonably apprize the skilled artisan of which polynucleotides fall within the claims.

However, Applicants are aware that there is a current policy at the PTO to reject as indefinite all claims reciting the "% identity" language where there is no explicit description of an algorithm and parameter settings in the specification. Thus, in the interest of facilitating prosecution, the % identity limitation does not appear in new claims 36-73. Thus, it is respectfully submitted that the rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The application is in a condition for allowance. Notice to that effect is earnestly solicited.

If, for any reason, a personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned directly at (202) 371-2627.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Kimberlin L. Morley
Attorney for Applicants
Registration No. 35,391

Date: September 3, 1998
1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005
(202) 371-2600

P:\USERS\KMORLEY\1488\071-01\071.amd